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Night Shift Work, Sleep Duration, Daytime Napping, and Breast Cancer Risk

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Highlights

- Night shift workers had an increased risk of breast cancer.
- Shorter or longer sleep duration also increased the risk.
- Night shift work and longer sleep duration synergically increased the risk.

Abstract

Objectives: Sleep habits vary among different countries, and sleep problems may cause various health problems. The aim of our study was to evaluate the separate and combined associations of night shift work, sleep duration, and daytime napping with breast cancer risk among Chinese.

Methods: This study conducted face-to-face interviews with 712 women diagnosed with incident invasive breast cancer before treatment and 742 age-matched controls. Information on sleep habits, demographic characteristics and suspected or established risk factors of breast cancer were collected from the two groups. Multivariate logistic regression models were used to estimate the odds ratios (OR) and 95% confidence intervals (CI).

Results: Night shift work was associated with an increased risk of breast cancer [OR (95%CI): 1.34 (1.05-1.72)]. Compared to women with sleep duration of 6.1-8.9 h/day, women who had shorter (≤6.0 h/day) [OR (95%CI): 1.53 (1.10-2.12) and longer

(≥9.0 h/day) sleep duration [OR (95% CI): 1.59 (1.17-2.17)] had an increased risk of breast cancer. In addition, daytime napping was associated with a reduced risk of breast cancer among night shift workers [OR (95% CI): 0.57 (0.36-0.90)] but no association was found among women who never had night shift work [OR (95% CI): 1.01 (0.75-1.35)] (*P* for interaction = 0.054). Night shift work and longer sleep duration also synergistically increased breast cancer risk [OR (95% CI): 3.69 (1.94-7.02)] (*P* for interaction = 0.009).

Conclusions: Sleep problems, including night shift work, shorter and longer sleep duration are associated with an increased breast cancer risk. In particular, the combined effects of night shift work with never daytime napping or longer sleep duration are greater than the independent effects.

Key words: night shift work; 24-hour sleep duration; daytime napping; breast cancer; interaction

1. Introduction

Breast cancer is the most common malignancy among women worldwide [1]. However, the known risk factors only explain a small proportion of the whole incidence of breast cancer [2]. Night shift work has been suggested to be linked with breast cancer [3,4]. The International Agency for Research on Cancer (IARC) classified night shift work as a probable cause of breast cancer (group 2A) [5]. However, there were also some findings with no association [6,7]. The inconsistency may be partially attributed to differences in night shift work assessment, study design, recall bias, and incomplete adjustment for confounding factors [8].

The above reasons may not be sufficient to explain the inconsistent association between night shift work and breast cancer risk. Night shift work is not only related to light exposure at night but also to sleeping duration. Whether there is enough sleeping time to compensate the time of night shift work may also be associated with breast cancer risk. Some studies have investigated the association between sleep duration and breast cancer risk. A significant association was found in most [9-12] but not all [13-15] of these studies. Considering that sleeping duration is likely to be related to night shift work, it is worthwhile to assess the combined effect of night shift work and sleeping duration on breast cancer risk. To our knowledge, only one study examined these two factors simultaneously with breast cancer risk [12].

In addition, daytime napping is also closely linked with sleeping duration and night shift work. Two studies have explored the relationships between daytime napping and

the risks of breast or other cancers. However, the both studies were conducted in Europe [16,17]. Daytime napping is not as common as in China and may indicate an unhealthy condition in most western countries [18]. Considering that the majority of Chinese have a daytime nap habit, the current study investigated the associations between night shiftwork, 24-hour sleep duration, daytime napping, and breast cancer risk as well as the joint effects of these sleep habits on breast cancer risk in Guangzhou, China.

2. Material and Methods

2.1. Study population

Female patients with newly histologically diagnosed primary breast cancer between July 2010 and March 2012 in the First- and Second-Affiliated Hospitals and Sun Yat-sen University Cancer Center, Guangzhou, China, were consecutively included in this study. Incident cases were immediately interviewed after admission and before treatment. Women with metastasized breast cancer or previous history of any cancers were excluded. A total of 712 eligible breast cancer cases completed face-to-face interviews with response rates ranging from 75% to 85% depending on different hospitals. Of the 712 cases, 661 (92.8%) cases answered the question of night shift work, 654 (91.9%) cases answered the question of 24-hour sleep duration, and 658 (92.4%) cases answered the question about daytime napping.

Controls were recruited from women who attended a health checkup in the same hospitals as the breast cancer cases during the same period, and were frequency-matched to cases by 5-year age groups. Women with major chronic diseases or who self-reported a history of cancer were excluded. Of the eligible controls, 742 (78.2%) completed in-person interviews. The response rates for the sleep-related variables were comparable to those among the breast cancer cases: 714 (96.2%) for night shift work; 667 (89.9%) for 24-hour sleep duration; and 674 (90.8%) for daytime napping.

All subjects must have resided in Guangzhou area for at least 5 years. All study participants signed informed consent. The study was approved by the Ethical Committee of the School of Public Health at Sun Yat-sen University.

2.2. Data collection

Cases and controls were interviewed face to face by trained interviewers using the same questionnaire. The questionnaire asked about the following information: demographic characteristics, menstrual and reproductive history, family history of breast cancer, physical activity, and sleep habits including night shift work, 24-hour sleep duration, and daytime napping. Height and weight were measured by the nurses on admission to the hospital. The clinical characteristics of breast cancer cases were extracted from medical records. Estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) status were reviewed and

determined by pathologists using immunohistochemistry tests. The definitions of ER, PR, and HER2 status were previously described in detail [19].

2.3. Sleep-related variables

For sleep-related variables, participants were asked about the following questions: 1) In your lifetime (adulthood), have you ever engaged in night shift work or other activities at night, at least once a week and last for six months or more (yes vs. no)? Night shift work or other activities at night was defined as being awake or working between midnight and 6:00 AM; 2) In the last 10 years, on average, how many hours did you sleep per 24 hours, including sleep hours at nighttime and during daytime? 24-hour sleep duration was categorized into three categories (≤6.0, 6.1-8.9, ≥9.0 h/day), and 6.1-8.9 h/day was used as the reference category; 3) In your lifetime (adulthood), have you ever taken daytime naps regularly, at least three days per week, and last for six months or more (yes vs. no)?

2.4. Statistical analysis

Differences in demographic characteristics and suspected or established risk factors of breast cancer between cases and controls were tested using χ^2 test for categorical variables, e.g. education, or Student's t-test for continuous variables, e.g. age. Multivariate logistic regression models were used to assess the associations between

sleep-related variables and breast cancer risk. The multivariate models were adjusted for age (continuous) and potential risk factors of breast cancer, including education (college or above, senior high school vs. junior high school), body mass index (BMI) (≥25.0, 23.0-24.9 vs. <23.0), age at menarche (>12 vs. ≤12), parity (≥1 vs. 0), menopausal status (postmenopausal vs. premenopausal, postmenopausal was defined as the absence of menstrual periods for 12 months), breastfeeding (ever vs. never), physical activity (≥18, 3~ <18, vs. < 3 Met-h/w/y), and family history of breast cancer (yes vs. no). Sleep-related variables were also included for mutual adjustment.

To assess the joint effects of night shift work, sleep duration, and daytime napping, participants were cross-classified by these three sleep-related variables. Stratified analyses were also performed to assess whether the associations between these sleep-related variables and breast cancer risk were modified by menopausal status, HER2, ER, and PR status, and clinical stages of breast cancer. To test the interactions between sleep factors and menopausal status, interaction terms were included in multivariate logistic regression models. Statistical tests were two-sided with $P < 0.05$ as significance level. All statistical analyses were performed using SPSS 13.0 (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Characteristics of cases and controls

The mean age was 47.6 [standard deviation (SD) = 11.1] years for cases and 47.4 [SD = 11.0] years for controls (P = 0.716) (Table 1). Compared with controls, cases were less educated, less physically active and had higher BMI. Cases and controls were comparable in other aspects, including marital status, age at menarche, menopausal status, age at menopause, parity, breastfeeding, and family history of breast cancer.

3.2. Associations between sleep-related variables and breast cancer risk

Among all subjects, 33.0% cases and 26.2% controls reported ever having night shift work [OR (95% CI): 1.34 (1.05-1.72)]. Women who reported shorter [OR (95% CI): 1.53 (1.10-2.12)] or longer sleep duration [OR (95% CI): 1.59 (1.17-2.17)] had an increased risk of breast cancer. Daytime napping was associated with a reduced risk of breast cancer [OR (95% CI): 0.83 (0.65-1.06)] (Table 2). The results were essentially unchanged in age-adjusted or multivariate-adjusted models, as well as after adjustment for other sleep-related variables.

3.3. Interactions between sleep-related variables

A significant interaction was found between night shift work and 24-hour sleep duration (P for interaction = 0.009). Among women who reported never having night shit work, no association between sleep duration and breast cancer risk was observed.

In contrast, both shorter [OR (95% CI): 1.83 (1.03-3.25)] and longer sleep duration [OR (95% CI): 3.69 (1.94-7.02)] was associated with a significantly increased risk of breast cancer among women who reported ever having night shift work. Daytime napping was associated with a reduced risk of breast cancer among night shift workers [OR (95% CI): 0.57 (0.36-0.90)] but no association was observed anong women who never had night shift work [OR (95% CI): 1.01 (0.75-1.35)], and the interaction was marginally significant (*P* for interaction = 0.054). Among women who never had daytime napping, shorter sleep duration [OR (95% CI): 1.71 (1.10-2.68)] but not longer sleep duration [OR (95% CI): 1.49 (0.79-2.81)] was associated with a significantly increased breast cancer risk. In contrast, among women who ever had daytime napping, longer sleep duration [OR (95% CI): 1.63 (1.14-2.34)] but not shorter sleep duration [OR (95% CI): 1.22 (0.73-2.03)] was associated with a significantly increased breast cancer risk. However, no significant interaction was observed (Table 3).

3.4. Stratified associations between sleep-related variables and breast cancer risk by menopausal status and clinical characteristics

Table 4 presents results of multivariate-adjusted ORs for the associations between sleep-related variables and breast cancer risk stratified by menopausal status, HER2, ER, PR status, and clinical stages. Results for night shift work were similar across HER2 status, PR status and clinical stages. A slightly stronger association between

night shift work and breast cancer risk was observed among women with ER positive [OR (95% CI): 1.48 (1.13-1.93)], whereas no association was found among ER negative women (*P* for heterogeneity = 0.030). A significant association between sleep duration and breast cancer risk was only observed among premenopausal women [shorter sleep duration ≤6.0 h/day, OR (95% CI): 2.24 (1.39-3.60); longer sleep duration ≥9.0 h/day, OR (95% CI): 1.51 (1.03-2.20)]. The interaction between shorter sleep duration and menopausal status was statistically significant (*P* for interaction = 0.047). The association between daytime napping and breast cancer risk was not modified by menopausal status, clinical characteristics or stages of breast cancer.

4. Discussion

This study found that women who ever had night shift work had an increased risk of breast cancer. Compared to those who had normal sleep duration, women who had shorter or longer sleep duration had a significantly increased risk, particularly for premenopausal women. In addition, daytime napping was associated with a marginally reduced risk of breast cancer among night shift workers, but not among the subjects with no night shiftwork.

4.1. Night shift work and breast cancer risk

Our results showed a significantly increased risk of breast cancer in night shift workers, which are consistent with findings from most previous studies [3,4,20]. However, no association was reported in the Shanghai Women's Health study, the only previous study on night shift work and breast cancer conducted in China [6]. One possible explanation for the inconsistency could be due to the difference in age and/or menopausal status of the study subjects: only less than 30% were premenopausal women (age range 40-70 years) in the Shanghai Women's Health study; whereas more than 60% were premenopausal women (age range 22-85 years) in the present study. Meanwhile, the present study found that the increased risk associated with night shift work was more apparent among premenopausal women than postmenopausal women (Table 4), suggesting that the results from the two studies in China were consistent to some extent.

4.2. Sleep duration and breast cancer risk

At least seven observational studies have investigated the association between sleep duration and breast cancer risk with inconsistent results [9-15,21]. In general, short sleep duration was associated with an increased risk of breast cancer, and longer duration with a decreasing risk [9,10,14]. However, these results are contradictory with those from a population-based case-control study, which reported that increasing sleep duration but not short sleep duration was associated with an increased breast cancer risk [11]. No association was observed for shorter or longer sleep duration in

the other three studies [12,13,15]. The possible explanations for the inconsistent results include different study population and study designs, and different definitions of sleep-related variables. Another explanation could be due to not taking into account of other sleep-related variables, such as night shift work and daytime napping, considering that the present study showed that night shift work had significant interaction with sleep duration and daytime napping on breast cancer risk.

4.3. Potential biological pathways linking sleep habits to breast cancer

The mechanisms of sleep habits' effect on breast cancer are complicated and may involve a number of biological processes and mechanisms, including circadian disruption, exposure to light at night, and lifestyles [22]. Night shiftwork usually leads both exposure to light at night and circadian disruption [23], which suppresses melatonin production [13,14,24]. Melatonin can inhibit severe DNA damage, promote DNA repair, and control proliferation of cancer cells [25]. Urinary levels of melatonin and its endproduct of 6-sulfatoxymelatonin have been found to be inversely associated with breast cancer risk [3,13,26]. These findings suggest that our results of positive associations of night shift work, shorter sleep duration, and their combination with breast cancer risk were biologically plausible. In addition, melatonin has anti-estrogenic effect and inhibits proliferation of hormone responsive breast cancer cells, especially ER positive breast cancer cells [27], supporting the finding that night shift work was associated with a significantly increased risk of ER positive but not ER

negative breast cancer observed in our study (Table 4). Moreover, the finding that the increased risk associated with night shift work was more apparent among premenopausal than postmenopausal women can be explained by the facts of the anti-estrogenic effect of melatonin [27], and higher circulating estrogen levels among premenopausal as compared to postmenopausal women [28]. We also found that longer sleep duration was associated with a significantly increased risk of breast cancer. One possible reason is that people with longer sleep duration may suffer from weak immunity or ill condition [29] and be susceptible to breast cancer.

Circadian disruption induced by night shiftwork also alters the expression of clock-controlled genes, which are related to cell-cycle regulation, cell proliferation and apoptosis [22,30]. A series of clock genes have been identified [31] and the functions have been confirmed in mice [32]. A few numbers of epidemiologic studies have shown significant associations of the polymorphisms in the clock genes with breast cancer risk [33-35]. Furthermore, circadian disruption has been linked to epigenetic modification, which is closely related to cell proliferation and tumorigenesis [36]. It was found that the methylation levels of interferon gamma and Alu repetitive elements in peripheral blood DNA were significantly lower among night shift workers than day workers [37]. These effects of circadian disruption may occur together with or independently of melatonin [31,38]. The present study was not able to find out specific mechanisms, but it did suggest that circadian misalignment may play a more important role in breast carcinogenesis than sleep duration, because the association of

sleep duration with breast cancer risk was only observed among night shift workers (Table 3).

4.4. Daytime napping and breast cancer risk

We found a marginally significant inverse association between daytime napping and breast cancer risk. A few studies have explored this association [16,17]. In the Million Women Study, daytime napping was found to be associated with an increased risk of breast cancer after the first four years of follow up, but no association with seven years of follow up [16]. Ruesten et al. investigated the association between daytime napping and incidence of chronic diseases, including cancers, and found that daytime napping was inversely associated with chronic disease risk among non-hypertensive participants, but positively associated with chronic diseases among hypertensive patients [17]. It was likely that hypertensive people who self-reported daytime sleep tended to have a worse health condition or poorer quality of night sleep, thus more susceptible to chronic diseases than non-hypertensive people [29]. It is difficult to compare the results of these previous studies with ours, because these studies were conducted in western countries where daytime napping is not as common as in China.

4.5. Study limitations

Our study has some limitations. Firstly, the study subjects were recruited from three hospitals, and there might be misclassification for diagnosis of breast cancer. However, it was confirmed that the same pathologic criterion was used. Secondly, recall bias cannot be completely ruled out, because the sleep behaviors were self-reported and it is possible that breast cancer patients may be more sensitive and reported exposure more readily than controls. However, women in this study were not likely to know the relationship between sleep habits and breast cancer risk. The results showed that both shorter and longer sleep duration increased breast cancer risk, which indicated that recalls of cases and controls may not have a specific direction. Thirdly, the hospital-based design might also lead to selection bias. However, the cases and controls were recruited from the same hospital during the same study period, and all subjects must have resided in Guangzhou area for at least 5 years. Therefore, they were likely to come from the same catchment area and resemble each other with regard to those selective factors that led to the hospital admission and use of the facilities, and were comparable to some extent. Thus, selection bias was minimized. Finally, there might be misclassification of daytime napping among night shift workers, who may consider sleep during the day after shiftwork as daytime napping. Although during the interview we did clarify to the participants that only a short sleep (< 2 hr) at noon should be considered as daytime napping we cannot completely exclude the possibility of misinterpretation and misclassification. We have conducted a stratified analysis by night shiftwork so that the effect of daytime napping on breast

cancer risk can be shown among subjects who had never had night shiftwork (Table 3).

5. Conclusion

This study examines the associations between sleep-related variables, including night shift work, 24-hour sleep duration, daytime napping, and breast cancer risk. Night shift work, shorter sleep duration and longer sleep duration is associated with an increased breast cancer risk. Daytime napping may counteract to some extent the effect of night shift work and short sleep duration on breast cancer risk. However, longer sleep duration may not compensate the effect of night shift work on breast cancer risk. Further study is warranted to confirm our results.

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Table 1 Characteristics of breast cancer cases and controls

Variables	**Cases** *N (%)*	**Controls** *N (%)*	***P*-Value**
Age (years)			
≤ 40	209 (29.4)	218 (29.4)	
41– 60	413 (58.0)	440 (59.3)	
≥61	90 (12.6)	84 (11.3)	0.729
Mean age ± SD	47.6±11.1	47.4±11.0	0.716

Education			
Junior high school or below	347 (48.7)	281 (37.9)	
Senior high school	183 (25.7)	255 (34.4)	
College or above	166 (23.3)	197 (26.5)	**<0.001**
Unknown	16 (2.3)	9 (1.2)	
Body mass index (BMI) (kg/m^2)			
< 23.0	381 (53.5)	434 (58.5)	
23.0–24.9	151 (21.2)	135 (18.2)	
≥25.0	168 (23.6)	161 (21.7)	0.145
Unknown	12 (1.7)	12 (1.6)	
Mean BMI ± SD	23.0±3.2	22.5± 3.1	**0.006**
Marital status			
Never married	23 (3.2)	29 (3.9)	
Married/living as married	639 (89.8)	669 (90.2)	
Separated/widowed	49 (6.9)	41 (5.5)	0.460
Unknown	1 (0.1)	3 (0.4)	
Age at menarche (years)			
≤12	85 (11.9)	99 (13.3)	

>12	620 (87.1)	638 (86.0)	0.434
Unknown	7 (1.0)	5 (0.7)	
Menopausal status			
Premenopausal	449 (63.1)	462 (62.3)	
Postmenopausal	260 (36.5)	280 (37.7)	0.675
Unknown	3 (0.4)	0 (0.0)	
Age at menopause (years)[a]			
≤45	40 (15.4)	50 (17.9)	
46–50	105 (40.4)	128 (45.7)	
≥51	110 (42.3)	93 (33.2)	0.115
Unknown	5 (1.9)	9 (3.2)	
Parity			
0	52 (7.3)	58 (7.8)	
≥1	659 (92.6)	682 (91.9)	0.706
Unknown	1 (0.1)	2 (0.3)	
Physical activity			
< 3 Met-h/w/y	388 (54.5)	352 (47.4)	
3 ~ < 18 Met-h/w/y	166 (23.3)	191 (25.7)	

≥ 18 Met-h/w/y	111 (15.6)	157 (21.2)	**0.005**
Unknown	47 (6.6)	42 (5.7)	
Breastfeeding			
Never	115 (16.2)	139 (18.7)	
Ever	586 (82.3)	594 (80.1)	0.205
Unknown	11 (1.5)	9 (1.2)	
Family history of breast cancer			
Absent	671 (94.2)	709 (95.6)	
Present	27 (3.8)	19 (2.6)	0.179
Unknown	14 (2.0)	14 (1.9)	

[a]Postmenopausal women only.

Table 2 Age-adjusted and multivariate-adjusted odds ratios for the associations between sleep habits and breast cancer risk

Variables	Cases *N* (%)	Controls *N* (%)	OR[a] (95% CI)	OR[b] (95% CI)	OR[c] (95% CI)
Night shift work					
never	443 (67.0)	527 (73.8)	1.00 (reference)	1.00 (reference)	1.00 (reference)
ever	218 (33.0)	187 (26.2)	**1.39 (1.10-1.75)**	**1.37 (1.07-1.74)**	**1.34 (1.05-1.72)**
24-hour sleep duration					
≤6.0	116 (17.7)	85 (12.8)	**1.62 (1.18-2.21)**	**1.63 (1.18-2.25)**	**1.53 (1.10-2.12)**
6.1-8.9	409 (62.6)	485 (72.7)	1.00 (reference)	1.00 (reference)	1.00 (reference)
≥9.0	129 (19.7)	97 (14.5)	**1.58 (1.18-2.12)**	**1.55 (1.14-2.10)**	**1.59 (1.17-2.17)**

P-continuous			0.646	0.886	0.447
Daytime napping					
never	293 (44.5)	254 (37.7)	1.00 (reference)	1.00 (reference)	1.00 (reference)
ever	365 (55.5)	420 (62.3)	**0.75 (0.61-0.94)**	0.82 (0.65-1.04)	0.83 (0.65-1.06)

[a]Adjusted for age.

[b]Adjusted for age, education, BMI, age at menarche, menopausal status, parity, physical activity, breastfeeding and first-degree family history of breast cancer.

[c]Adjusted for age, education, BMI, age at menarche, menopausal status, parity, physical activity, breastfeeding, family history of breast cancer, and other sleep factors (24-hour sleep duration, night shift work or daytime napping).

Abbreviations: OR: odds ratio; CI: confidence interval.

Table 3 Joint effects of night shift work, 24-hour sleep duration, and daytime napping on breast cancer risk

Stratified Variables		Cases *N* (%)	Controls *N* (%)	OR[a] (95%CI)	OR[b] (95%CI)
Night shift work	24-hour sleep duration				
never	≤6.0	69 (15.6)	56 (11.4)	1.41 (0.94-2.11)	1.41 (0.94-2.12)
	6.1-8.9	289 (66.1)	356 (72.4)	1.00 (reference)	1.00 (reference)
	≥9.0	79 (18.1)	80 (16.3)	1.16 (0.81-1.67)	1.16 (0.81-1.67)
ever	≤6.0	47 (21.9)	29 (16.6)	**2.08 (1.18-3.64)**	**1.83 (1.03-3.25)**
	6.1-8.9	119 (55.3)	129 (73.7)	1.00 (reference)	1.00 (reference)
	≥9.0	49 (22.5)	17 (9.7)	**3.22 (1.72-6.04)**	**3.69 (1.94-7.02)**

P for interaction[c]				0.473	0.480
P for interaction[d]				**0.009**	**0.009**
Night shift work	Daytime napping				
never	never	179 (40.8)	186 (37.3)	1.00 (reference)	1.00 (reference)
	ever	260 (59.2)	312 (62.7)	1.00 (0.75-1.33)	1.01 (0.75-1.35)
ever	never	113 (52.1)	68 (38.6)	1.00 (reference)	1.00 (reference)
	ever	104 (47.7)	108 (61.4)	**0.62 (0.40-0.95)**	**0.57 (0.36-0.90)**
P for interaction				**0.031**	**0.054**
Daytime napping	24-hour sleep duration				
never	≤6.0	80 (27.7)	47 (18.9)	**1.81 (1.16-2.83)**	**1.71 (1.10-2.68)**
	6.1-8.9	180 (62.3)	181 (72.7)	1.00 (reference)	1.00 (reference)

	≥9.0	29 (10.0)	21 (8.4)	1.56 (0.83-2.91)	1.49 (0.79-2.81)
ever	≤6.0	36 (9.9)	38 (9.1)	1.23 (0.74-2.04)	1.22 (0.73-2.03)
	6.1-8.9	229 (62.7)	304 (72.7)	1.00 (reference)	1.00 (reference)
	≥9.0	100 (27.4)	76 (18.2)	**1.64 (1.14-2.34)**	**1.63 (1.14-2.34)**
P for interaction[c]				0.267	0.266
P for interaction[d]				0.663	0.609

[a]Adjusted for age, education, BMI, age at menarche, menopausal status, parity, physical activity, breastfeeding, and first-degree family history of breast cancer.

[b]Adjusted for age, education, BMI, age at menarche, menopausal status, parity, physical activity, breastfeeding, first-degree family history of breast cancer, and other sleep factors (24-hour sleep duration, night shift work or daytime napping).

[c]Between daytime napping or night shift work and 24-hour sleep duration (≤6.0 h/day vs. 6.1-8.9 h/day)

[d]Between daytime napping or night shift work and 24-hour sleep duration (≥9.0 h/day vs. 6.1-8.9 h/day)

Abbreviations: OR: odds ratio; CI: confidence interval.

ultivariate-adjusted odds ratios for the associations between night shift work, 24-hour sleep duration, daytime napping, and l

stratified by menopause status, HER2, ER, PR status, and clinical stages

ied / les	Night shift work			24-hour sleep duration			Daytime Nappin		
		Cases /Controls	OR[a] (95%CI)		Cases /Controls	OR[a] (95%CI)		Cases /Controls	OR[a] (
al status									
pausal	never	278/332	1.00 (reference)	≤6.0	64/32	**2.24 (1.39-3.60)**	never	184/164	1.00 (r
	ever	144/110	**1.47 (1.07-2.01)**	6.1-8.9	272/323	1.00 (reference)	ever	236/260	0.93 (0
				≥9.0	82/65	**1.51 (1.03-2.20)**			
opausal	never	162/195	1.00 (reference)	≤6.0	52/53	1.12 (0.69-1.82)	never	107/90	1.00 (r
	ever	74/77	1.17 (0.77-1.80)	6.1-8.9	134/162	1.00 (reference)	ever	128/160	0.75 (0
				≥9.0	47/32	1.59 (0.92-2.74)			
raction			0.263			**0.047**[b] /0.781[c]			0.606
us									
	never	294/527	1.00 (reference)	≤6.0	68/85	1.30 (0.90-1.90)	never	189/254	1.00 (r
	ever	146/187	**1.39 (1.05-1.83)**	6.1-8.9	278/485	1.00 (reference)	ever	249/420	0.85 (0
				≥9.0	89/97	**1.58 (1.12-2.23)**			
l/	never	131/527	1.00 (reference)	≤6.0	41/85	**1.94 (1.23-3.07)**	never	90/254	1.00 (r

ever	66/187	1.35 (0.94-1.94)	6.1-8.9	117/485	1.00 (reference)	ever	106/420	0.82 (0
			≥9.0	37/97	**1.70 (1.09-2.67)**			
erogeneity		0.539			0.166			0.848
never	130/527	1.00 (reference)	≤6.0	38/85	**1.95 (1.22-3.13)**	never	83/254	1.00 (r
ever	53/187	1.10 (0.74-1.62)	6.1-8.9	104/485	1.00 (reference)	ever	97/420	0.76 (0
			≥9.0	37/97	**1.86 (1.17-2.95)**			
never	298/527	1.00 (reference)	≤6.0	73/85	1.32 (0.92-1.91)	never	199/254	1.00 (r
ever	160/187	**1.48 (1.13-1.93)**	6.1-8.9	293/485	1.00 (reference)	ever	259/420	0.85 (0
			≥9.0	89/97	**1.52 (1.09-2.14)**			
erogeneity		**0.030**			0.143			0.662
never	142/527	1.00 (reference)	≤6.0	39/85	1.46 (0.92-2.32)	never	98/254	1.00 (r
ever	66/187	1.34 (0.93-1.93)	6.1-8.9	129/485	1.00 (reference)	ever	107/420	0.73 (0
			≥9.0	35/97	1.35 (0.85-2.14)			
never	285/527	1.00 (reference)	≤6.0	72/85	**1.51 (1.05-2.18)**	never	183/254	1.00 (r
ever	147/187	**1.39 (1.05-1.82)**	6.1-8.9	267/485	1.00 (reference)	ever	249/420	0.88 (0
			≥9.0	91/97	**1.74 (1.24-2.44)**			

erogeneity			0.455			0.642			0.310
ages									
l	never	223/527	1.00 (reference)	≤6.0	71/85	**1.90 (1.30-2.80)**	never	149/254	1.00 (r
	ever	120/187	**1.47 (1.09-1.99)**	6.1-8.9	206/485	1.00 (reference)	ever	189/420	0.84 (0
				≥9.0	59/97	**1.50 (1.02-2.20)**			
y	never	201/527	1.00 (reference)	≤6.0	42/85	1.22 (0.79-1.87)	never	131/254	1.00 (r
	ever	89/187	1.22 (0.89-1.67)	6.1-8.9	181/485	1.00 (reference)	ever	160/420	0.81 (0
				≥9.0	66/97	**1.81 (1.24-2.63)**			
erogeneity			0.155			0.095			0.559

for age, education, BMI, age at menarche, menopausal status, parity, physical activity, breastfeeding, first-degree family hist
cer, and other sleep factors (24-hour sleep duration, night shift work or daytime napping).

menopausal and 24-hour sleep duration (≤6.0 h/day vs. 6.1-8.9 h/day).

menopausal and 24-hour sleep duration (≥9.0 h/day vs. 6.1-8.9 h/day).

ons: OR: odds ratio; CI: confidence interval; HER2: human epidermal growth factor receptor 2; ER: Estrogen receptor; PR:
ne receptor.